Clinical trial results:
A Study of the Safety and Efficacy of IMM-101 in Combination with Checkpoint Inhibitor Therapy in Patients with Advanced Melanoma

Summary

EudraCT number	2018-001346-34
Trial protocol	GB
Global end of trial date	02 December 2021

Results information

Result version number	v1 (current)
This version publication date	15 December 2022
First version publication date	15 December 2022

Trial information

Trial identification

Sponsor protocol code	IMM-101-015

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03711188
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Immodulon Therapeutics Ltd
Sponsor organisation address	6-9 The Square, Stockley Park, Uxbridge, United Kingdom, UB11 1FW
Public contact	Clinical Trial Information Desk, Immodulon Therapeutics Ltd, 0044 0203137 6346, info@immodulon.com
Scientific contact	Clinical Trial Information Desk, Immodulon Therapeutics Ltd, 0044 0203137 6346, info@immodulon.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 December 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 June 2021
Global end of trial reached?	Yes
Global end of trial date	02 December 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

• To evaluate Overall Response Rate (ORR) after a maximum of 18 months treatment, in patients with advanced melanoma receiving IMM-101 plus nivolumab. ORR in both previously untreated patients (cohort A) and in patients whose disease has progressed during PD-1 blockade (cohort B) will be evaluated using RECIST 1.1. ORR will also be assessed for subgroups based on PD-L1 status (positive or negative/undetermined) in cohort A patients.
• To evaluate the safety and tolerability of the combination of IMM-101 plus nivolumab in patients with advanced melanoma by examining the profile of adverse events experienced.

Protection of trial subjects:

IMM-101, in pancreatic cancer studies has been shown,when co-administered with gemcitabine, to provide clinically relevant survival benefits and improvements in progression free survival. The safety data indicated that this was achieved without significant additional toxicity. As such the risk/benefit for further evaluation in other cancer indications was considered favourable.
An interim data review was performed for cohort B patients.

Background therapy:

Nivolumab was to be given as 3 mg/kg intravenous (IV) infusion every 2 weeks, 240 mg IV infusion every 2 weeks or
480 mg IV infusion every 4 weeks, according to the prescribing information in both Cohort A and Cohort B.
If used on study for patients in Cohort B, ipilimumab was to be administered as a 3 mg/kg IV infusion over 90 minutes
every 3 weeks for a maximum of 4 doses, in accordance with the prescribing information

Evidence for comparator:

Not applicable - this was not a comparative study. I

Actual start date of recruitment	17 September 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 16
Worldwide total number of subjects	16
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0

Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	6
From 65 to 84 years	9
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Patients who provided informed consent participated in a Screening period of up to a maximum of 21 days to establish eligibility. Sixteen patients were deemed to have met the eligibility criteria and were treated between 04-Oct-2018 and 06-May-2021.

Pre-assignment

Screening details:

Twenty-two patients at 2 centres were consented and screened. Six patients failed to meet one or more of the specific inclusion criteria or met one or more exclusion criteria and were deemed screen failures.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort A

Arm description:

Patients in cohort A were treatment-naive and were required to have had a tumour sample (archived tissue in the last 3 months or newly obtained biopsy) that was adequate for PD-L1 assessment prior to enrolment.

Arm type	Experimental
Investigational medicinal product name	Heat killed whole cell M. obuense NCTC 13365
Investigational medicinal product code	IMM-101
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intradermal use

Dosage and administration details:

All patients in both cohorts of the study were to receive one dose of IMM-101 every 2 weeks for the first 3 doses followed by a rest period of 4 weeks, then every 2 weeks for the next 3 doses, and thereafter every 4 weeks.
IMM-101 (10 mg/mL) was to be administered as a single 0.1 mL intradermal injection (10 mg/mL) into the skin overlying the deltoid muscle, with the arm being alternated between each dose.

Arm title	Cohort B

Arm description:

Patients in cohort B were either currently on (or had previously received) treatment with an anti-PD-1 therapy (monotherapy or in combination) for advanced melanoma and had progressive disease by RECIST 1.1 after at least 3 doses of anti-PD-1 given as monotherapy or at least 2 doses of anti-PD-1 given in combination regimes and had not received any therapy since for advanced melanoma.

Arm type	Experimental
Investigational medicinal product name	Heat killed whole cell M. obuense NCTC 13365
Investigational medicinal product code	IMM-101
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intradermal use

Dosage and administration details:

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IMM-101 (10 mg/mL) was to be administered as a single 0.1 mL intradermal injection (10 mg/mL) into the skin overlying the deltoid muscle, with the arm being alternated between each dose.

Number of subjects in period 1	Cohort A	Cohort B
Started	11	5
Completed	4	0
Not completed	7	5
Disease progression	6	5
Adverse event, non-fatal	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Overall study
Reporting group description:	
All patients in either cohort who received at least one dose of IMM-101	

Reporting group values	Overall study	Total	
Number of subjects	16	16	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
median	68.5		
full range (min-max)	36 to 92	-	
Gender categorical Units: Subjects			
Female	5	5	
Male	11	11	

End points

End points reporting groups

Reporting group title	Cohort A

Reporting group description:

Patients in cohort A were treatment-naive and were required to have had a tumour sample (archived tissue in the last 3 months or newly obtained biopsy) that was adequate for PD-L1 assessment prior to enrolment.

Reporting group title	Cohort B

Reporting group description:

Patients in cohort B were either currently on (or had previously received) treatment with an anti-PD-1 therapy (monotherapy or in combination) for advanced melanoma and had progressive disease by RECIST 1.1 after at least 3 doses of anti-PD-1 given as monotherapy or at least 2 doses of anti-PD-1 given in combination regimes and had not received any therapy since for advanced melanoma.

Subject analysis set title	Cohort A PD-L1 Positive at screening
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subgroups of patients in cohort A were defined based on PD-L1 status (PD-L1 positive and PD-L1 negative/indeterminate) at Screening. For one patient PD-L1 status was unknown.

Subject analysis set title	Cohort A PD-L1 Negative/indeterminate at screening
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subgroups of patients in cohort A were defined based on PD-L1 status (PD-L1 positive and PD-L1 negative/indeterminate) at Screening.

The PD-L1 status of one patient was unknown

Primary: Safety

End point title	Safety[1]

End point description:

Incidence, frequency and severity of treatment emergent adverse events (TEAEs) throughout the study. This included all TEAEs, SAEs, treatment-related TEAEs, immune-related AEs, Grade 3 and above TEAEs and TEAEs leading to IMM-101 discontinuation or study withdrawal.

A total of 120 full doses of IMM-101 were administered to patients in cohort A and 30 full doses to patients in cohort B.

The median (range) total exposure to nivolumab per patient in cohort A was 3360 (360 to 11200) mg and per patient in cohort B was 880 (640 to 4020) mg.

Only one patient, Patient 01-201 in cohort B, received ipilimumab (one infusion of 175 mg).

End point type	Primary

End point timeframe:

From the point of Informed Consent until withdrawal from the study or the end of study assessment.

All 16 patients enrolled had at least one dose of IMM-101 and nivolumab.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There was no statistical analysis on this primary endpoint
Descriptive evaluation of efficacy and safety endpoints was performed using summary statistics for continuous data endpoints and frequency counts and percentages for categorical data endpoints. All study data were presented as data listings

End point values	Cohort A	Cohort B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	5		
Units: Events or patients				
Number of TEAEs	81	29		
Number of serious TEAEs	8	5		
Number of patients with TEAEs leading to withdrawa	1	0		
Number of patients with fatal TEAEs	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)[2]

End point description:

Overall Response Rate (ORR) was calculated from the Best overall Response (BOR) of patients as assessed by RECIST 1.1.

Due to the small number of patients in this study, the 95% CIs for the response rate estimates are correspondingly wide and hence results should be interpreted with caution.

The ORR was 73% (95% CI 39, 94) in cohort A. Two of these patients were complete responders. All patients in cohort B reported progressive disease.

End point type	Primary

End point timeframe:

From Informed consent until death, withdrawal from study or after a maximum of 18 months treatment (End of Study)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There was no statistical analysis on this primary endpoint
Descriptive evaluation of efficacy and safety endpoints was performed using summary statistics for continuous data endpoints and frequency counts and percentages for categorical data endpoints. All study data were presented as data listings

End point values	Cohort A	Cohort B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	5		
Units: percent				
number (not applicable)				
Complete Response	18	0		
Partial Response	55	0		
Stable Disease	9	0		
Progressive Disease	18	100		
Overall Response Rate	73	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival (PFS)

End point title	Progression free survival (PFS)

End point description:

Progression-free survival was defined as the time from Visit 1 (week 0) and the first confirmation of progression using RECIST 1.1 (confirmed or unconfirmed), or death from any cause (whichever occurred first). Progression was determined by the investigator using the CT or MRI scan or death due to any cause. Patients who died without reporting progression were considered to have progressed on the date of their death.

The median PFS time for Cohort A was 10.2 months (95% CI 3 months, not evaluable [NE]). Over 50% of the cohort A patients were progression-free for at least 9 months and 41% were progression-free for at least 18 months.

No patients in Cohort B had a response to treatment so median PFS was not evaluable.

End point type	Secondary

End point timeframe:

From Visit 1 (week 0) and the first confirmation of progression using RECIST 1.1 (confirmed or unconfirmed), or death from any cause (whichever occurred first).

End point values	Cohort A	Cohort B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	5		
Units: Patients who are progression free				
number (not applicable)				
PFS < or = 3 months	2	4		
PFS > 3 but < 6 months	1	1		
PFS >6 but < 9 months	3	0		
PFS >9 but < 12 months	1	0		
PFS > 12 but < 18 months	0	0		
PFS = or > 18 months	4	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

Overall survival was defined as the time from Visit 1 (week 0) until date of death from any cause. OS was calculated for the entire study duration, where patients without a death date were right censored at the date the patient was last known to be alive. Post-study survival information was collected until database lock, for subjects completing or withdrawing from the study and included in the analysis.

In cohort A, One patient died whilst on study and three patients died during post- study follow up. The remaining seven patients were known to be alive at last contact which varied between 55 days and 2.5 years post-study. The median OS time was not calculable for cohort A as less than 50% patients died.

In cohort B, all five patients died between 4 and 7 months after withdrawing from the study. The median OS time for patients in cohort B was 9.7 months (95% CI 6, NE).

End point type	Secondary

End point timeframe:

Overall survival was defined as the time from Visit 1 (week 0) until date of death from any cause. OS was calculated for the entire study duration, where patients without a death date were right censored at the date the patient was last known to be alive.

End point values	Cohort A	Cohort B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	5		
Units: Patients alive at various timepoints				
number (not applicable)				
OS < 3 months	1	0		
OS > 3 but < 6 months	0	0		
OS > 6 but < 9 months	1	2		
OS > 9 but < 12 months	0	2		
OS >12 but < 18 months	0	1		
OS = or > 18 months	9	0		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Overall Response Rate based on PD-L1 status at screening

End point title	Overall Response Rate based on PD-L1 status at screening

End point description:

For cohort A a subgroup analysis of overall response rate was conducted according to PD-L1 status at screening.
Objective response rate is calculated as the number of patients with a best objective response of complete response or partial response divided by the number of patients in the analysis set.

End point type	Other pre-specified

End point timeframe:

From informed consent to study completion or withdrawal

End point values	Cohort A PD-L1 Positive at screening	Cohort A PD-L1 Negative/indeterminate at screening		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	4		
Units: percent				
number (confidence interval 95%)	83 (36 to 100)	75 (19 to 99)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from the point of Informed Consent until withdrawal from the study or the end of study assessment.

Adverse event reporting additional description:

Treatment emergent adverse events (TEAEs) were defined as AEs occurring at or after the first IMM-101 dose These included all TEAEs, SAEs, treatment-related TEAEs, immune-related AEs, Grade 3 and above TEAEs and TEAEs leading to IMM-101 discontinuation or study withdrawal.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Safety Analysis Set

Reporting group description:

The Safety Analysis Set included all patients who received at least one dose of IMM-101, irrespective of compliance with eligibility and other protocol criteria.

Serious adverse events	Safety Analysis Set		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 16 (37.50%)		
number of deaths (all causes)	9		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Atrioventricular block			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chills			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Fatigue				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lethargy				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Epistaxis				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Dysphagia				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Pneumonia				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
Cortisol deficiency				

subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Wrist fracture			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal cord compression			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Safety Analysis Set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 16 (100.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
General disorders and administration site conditions			
Rash			
subjects affected / exposed	7 / 16 (43.75%)		
occurrences (all)	9		
Fatigue			
subjects affected / exposed	6 / 16 (37.50%)		
occurrences (all)	9		
Injection site erythema			
subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	6		
Pruritus			

subjects affected / exposed occurrences (all) Injection site swelling subjects affected / exposed occurrences (all) Injection site ulcer subjects affected / exposed occurrences (all) Chest pain subjects affected / exposed occurrences (all) Facial pain subjects affected / exposed occurrences (all) Influenza like illness subjects affected / exposed occurrences (all) Injection site vesicles subjects affected / exposed occurrences (all) Peripheral swelling subjects affected / exposed occurrences (all)	4 / 16 (25.00%) 5 3 / 16 (18.75%) 5 3 / 16 (18.75%) 4 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1		
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	 1 / 16 (6.25%) 1		
Reproductive system and breast disorders Bartholin's cyst subjects affected / exposed occurrences (all)	 1 / 16 (6.25%) 1		
Respiratory, thoracic and mediastinal disorders Nasal polyps subjects affected / exposed occurrences (all)	 1 / 16 (6.25%) 1		
Injury, poisoning and procedural			

complications Head injury subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Cardiac disorders Bundle branch block right subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Nervous system disorders Dyspnoea subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Hypoaesthesia subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 3 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1		
Eye disorders Eye haemorrhage subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Breath odour subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Mouth ulceration subjects affected / exposed occurrences (all) Nausea	3 / 16 (18.75%) 6 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1		

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Toothache			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Hepatobiliary disorders			
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Pain of skin			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Psoriasis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Rash erythematous			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Swelling face			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Vitiligo			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	4		
Hyperthyroidism			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Alanine aminotransferase increased			

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
coronavirus			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Haemoglobin decreased			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Vitamin D decreased			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Arthralgia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Pain in jaw			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Cystitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Lower respiratory tract infection			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Oral infection			

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 December 2019	The original protocol (Version 1.0) was dated 09 April 2018. Version 2.0 of the protocol, dated 16 December 2019, was considered to be a substantial protocol amendment and included: * Amendment of the inclusion criterion that specified the number of doses of prior treatment with anti-PD-1 therapy that were required for cohort B of the study. * Removal of the exclusion criterion that limited the number of treatment regimens allowed prior to anti-PD-1 therapy to one, for patients enrolling in cohort B of the study. * Amendment of dosing schedule of nivolumab to accommodate an investigator choice between 3 mg/kg every 2 weeks, 240 mg every 2 weeks or 480 mg every 4 weeks. * Change of time between end of other investigational product and first study dose from 4 weeks to 3 weeks. * Number of sites increased from 1 to 3-4 sites

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
02 March 2020	Due to the COVID-19 pandemic, recruitment was suspended at both study sites in March 2020 and was not resumed	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The ORR in Cohort A compared favourably with those seen in a similar population treated with nivolumab only, although the sample size is small in this non-comparative study and this finding would need to be confirmed in larger studies.

Notes: